ANTİDEPRESANLAR

99. BÖLÜM

Masum ÖZTÜRK[1]

GİRİŞ

Son 30 yıl boyunca, çocuklarda ve ergenlerde psikiyatrik bozuklukların tedavisinde reçeteli ilaç kullanımında çarpıcı bir artış görülmüştür. Bu artış, çocukluk çağındaki psikiyatrik hastalıkların epidemiyolojisi, etiyolojisi ve nörobilimi konusundaki ilerlemelerle ve ilaç tedavisinin bir tedavi yöntemi olarak kabul edilmesiyle desteklenmiştir. Birçok nöropsikiyatrik bozukluk çocukluk çağında ortaya çıkmakta ve yaşam boyunca devam etmekte olup erken tedavi müdahalelerinin uzun dönemde daha olumlu sonuçlar verdiği ortaya konmuştur. Psikiyatrik hastalıklarının tanı, tedavi ve yörüngesinde yetişkinler ve çocuklar arasında önemli farklılıklar vardır (1).

Piyasada birçok antidepresan bulunmaktadır ve bu ilaçlar; depresif bozukluklar, anksiyete bozuklukları, yeme bozuklukları, dikkat eksikliği hiperaktivite bozukluğu ve enürezis de dâhil olmak üzere çok çeşitli tanılar için reçete edilmektedir. Antidepresanlar etki mekanizmalarına göre sınıflandırılır ancak ilaç seçiminde hastanın tanısı, hastanın yaşı ve ilacın yan etki profili göz önüne alınmalıdır. Ayrıca, bir ilacın belirli bir tanı ve yaş aralığı için FDA onaylı olup olmadığını ya da endikasyon dışı kullanılıp kullanılmadığına dikkat edilmelidir (1).

Son birkaç dekatta, çocuk-ergen depresyon ve anksiyetesinde seçici serotonin geri alım inhibitörleri (SSGİ)'nin ve serotonin noradrenalin geri alım inhibitörleri (SNGİ)'nin kullanımına dair kanıtlar artmaktadır. Antidepresanların, pediatrik depresyon, yaygın anksiyete bozukluğu (YAB), ayrılma anksiyetesi bozukluğu (AAB), sosyal anksiyete bozukluğu (SAB) ve çocuklukta ortaya çıkan obsesif kompulsif bozukluk (OKB) için etkinliği kanıtlanmıştır (2). Genel olarak, SSGİ veya SNGİ dışındaki antidepresanların 18 yaşın altındaki bireylerde depresyon veya anksiyete için kullanımı ile ilgili az sayıda çalışma bulunmaktadır.

Çocuk ve ergen depresyonunda, SSGİ ve SNGİ'ler ile ilgili hem pozitif hem negatif sonuçlar içeren çok sayıda randomize plasebo kontrollü çalışma bulunmaktadır. Bazı otörler, çocuk ve ergen depresyonunda başarısız olan çalışmaların sebebinin ilaçların etkinliğinin az olmasından çok çalışmaların tasarımlarından kaynaklandığını belirtmektedir (3). Fluoksetin çocuk ve ergen depresyonunda kanıt düzeyi en yüksek antidepresandır. Bu yüzden potansiyel ilaç etkileşimine göre ve daha önce yeterli doz ve süre ile başarısız tedavi öyküsünün bulunmadığı durumlarda ilk sırada tercih edilir. Essitalopram, majör depresif bozukluk (MDB)'ta 12 yaş ve üstü çocuklarda ve ergenlerde değerlendirilmiş ve etkili ve güvenli olduğu bildirilmiştir. Diğer birinci basamak antidepresanlar arasında sertralin bulunur (4). Majör depresyonu olan çocuklarda ve ergenlerde, sertralin ve sitalopram ile yapılan plasebo kontrollü iki çalışma ve paroksetin ile yapılan üç plasebo kontrollü çalışmada bu ilaçların tedavide etkin olmadığı gösterilmiştir. FDA 2003 yılında paroksetinin çocuklarda ve ergenlerde depresyon tedavisinde kullanılmamasını önermiştir. Paroksetin ile ya-

[1] Uzman Doktor, Kızıltepe Devlet Hastanesi, Çocuk ve Ergen Ruh Sağlığı ve Hastalıkları Kliniği, masumozturk@hotmail.com
ORCID iD: 0000-0002-9989-7051

almaktadır. Depresif bozuklukta hem çocuklarda hem ergenlerde FDA onayı alan tek ilaç fluoksetindir. Essitalopram MDB tedavisinde ergenlerde FDA onayı diğer ilaçtır. Çocuklarda ve ergenlerde depresif bozukluğun farmakolojik tedavisinde ilk sırada seçilecek ajan kanıt düzeyi en yüksek olan fluoksetindir. Duloksetin anksiyete bozuklukları içinde yer alan yaygın anksiyete bozukluğu tedavisi için FDA onayı alan tek ilaçtır. Fluoksetin, sertralin, fluvoksamin ve klomipramin çocuklarda ve ergenlerde FDA onayı alan ilaçlardır. Çocuklarda ve ergenlerde antidepresan ilaçlar düşük dozlarda başlanmalı, yavaş titre edilmeli ve yan etkiler açısından özellikle tedavinin ilk aşamasında hastalar sık izlenmelidir. SNGİ grubunda yer alan venlafaksin MDB tedavisinde diğer tedavilere yanıt vermeyen durumlarda etkin bulunmuştur fakat olası yan etkileri nedeniyle ilk sıra tedavisinde yer almamaktadır. Trisiklik antidepresanların etkinliği ile ilgili kanıt düzeyinin yetersiz olması ve olası yan etkileri nedeniyle çocuklarda ve ergenlerde genellikle tercih edilmemektedir.

KAYNAKÇA

1. Nazeer A. A review on psychopharmacology in children and adolescents. Journal of Alternative Medicine Research. 2017;9(1):43-53.
2. Giles LL, Martini DR. Challenges and promises of pediatric psychopharmacology. Academic pediatrics. 2016;16(6):508-18.
3. Bridge JA, Iyengar S, Salary CB, Barbe RP, Birmaher B, Pincus HA, et al. Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. Jama. 2007;297(15):1683-96.
4. Grover S, Avasthi A. Clinical practice guidelines for the management of depression in children and adolescents. Indian journal of psychiatry. 2019;61(Suppl 2):226-40.
5. Strawn JR, Prakash A, Zhang Q, Pangallo BA, Stroud CE, Cai N, et al. A randomized, placebo-controlled study of duloxetine for the treatment of children and adolescents with generalized anxiety disorder. Journal of the American Academy of Child & Adolescent Psychiatry. 2015;54(4):283-93.
6. Hussain FS, Dobson ET, Strawn JR. Pharmacologic treatment of pediatric anxiety disorders. Current treatment options in psychiatry. 2016;3(2):151-60.
7. The Pediatric OCD Treatment Study (POTS) Team. Cognitive-Behavior Therapy, Sertraline, and Their Combination for Children and Adolescents With Obsessive-Compulsive Disorder: The Pediatric OCD Treatment Study (POTS) Randomized Controlled Trial. JAMA. 2004;292(16):1969–76.
8. Walkup JT, Albano AM, Piacentini J, Birmaher B, Compton SN, Sherrill JT, et al. Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. New England Journal of Medicine. 2008;359(26):2753-66.
9. Compton SN, Walkup JT, Albano AM, Piacentini JC, Birmaher B, Sherrill JT, et al. Child/adolescent anxiety multimodal study (CAMS): rationale, design, and methods. Child and adolescent psychiatry and mental health. 2010;4(1):1.
10. March J, Silva S, Petrycki S, Curry J, Wells K, Fairbank J, et al. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. Jama. 2004;292(7):807-20.
11. March JS, Vitiello B. Clinical messages from the treatment for adolescents with depression study (TADS). American Journal of Psychiatry. 2009;166(10):1118-23.
12. Brent D, Emslie G, Clarke G, Wagner KD, Asarnow JR, Keller M, et al. Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy for adolescents with SSRI-resistant depression: the TORDIA randomized controlled trial. Jama. 2008;299(8):901-13.
13. Vitiello B, Emslie G, Clarke G, Wagner KD, Asarnow JR, Keller M, et al. Long-term outcome of adolescent depression initially resistant to SSRI treatment. The Journal of clinical psychiatry. 2011;72(3):388-96.
14. Strawn JR, Dobson ET, Giles LL. Primary pediatric care psychopharmacology: focus on medications for ADHD, depression, and anxiety. Current problems in pediatric and adolescent health care. 2017;47(1):3-14.
15. Patel DR, Feucht C, Brown K, Ramsay J. Pharmacological treatment of anxiety disorders in children and adolescents: a review for practitioners. Translational pediatrics. 2018;7(1):23-35.
16. Stahl, Stephen M. Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Applications. Fourth edition. Cambridge: Cambridge University Press, 2013.
17. Strawn JR, Geracioti L, Rajdev N, Clemenza K, Levine A. Pharmacotherapy for generalized anxiety disorder in adult and pediatric patients: an evidence-based treatment review. Expert opinion on pharmacotherapy. 2018;19(10):1057-70.
18. Richelson E. Interactions of antidepressants with neurotransmitter transporters and receptors and their clinical relevance. The Journal of clinical psychiatry. 2003;64:5-12.
19. Hiemke C, Härtter S. Pharmacokinetics of selective serotonin reuptake inhibitors. Pharmacology & therapeutics. 2000;85(1):11-28.
20. Zhou S-F. Polymorphism of human cytochrome P450 2D6 and its clinical significance. Clinical pharmacokinetics. 2009;48(12):761-804.
21. Christine J. Choe GJE, Taryn L. Mayes. Depression. Child and Adolescent Psychiatric Clinics of North America. 2012;21(4):807-29.
22. Katzung, Bertram G., Basic & Clinical Pharmacology. Fourteenth edition. New York: McGraw-Hill Medical, 2018.
23. Mandrioli R, Mercolini L, Raggi MA. Evaluation of the pharmacokinetics, safety and clinical efficacy of sertraline used to treat social anxiety. Expert opinion on drug metabolism & toxicology. 2013;9(11):1495-505.

24. Cipriani A, Purgato M, Furukawa TA, Trespidi C, Imperadore G, Signoretti A, et al. Citalopram versus other anti-depressive agents for depression. Cochrane Database of Systematic Reviews. 2012(7).
25. Marazziti D, Avella MT, Basile L, Mucci F, Dell'Osso L. Pharmacokinetics of serotonergic drugs: focus on OCD. Expert opinion on drug metabolism & toxicology. 2019;15(4):261-73.
26. Wagner KD, Robb AS, Findling RL, Jin J, Gutierrez MM, Heydorn WE. A randomized, placebo-controlled trial of citalopram for the treatment of major depression in children and adolescents. American Journal of Psychiatry. 2004;161(6):1079-83.
27. Rao N. The clinical pharmacokinetics of escitalopram. Clinical pharmacokinetics. 2007;46(4):281-90.
28. Søgaard B, Mengel H, Rao N, Larsen F. The pharmacokinetics of escitalopram after oral and intravenous administration of single and multiple doses to healthy subjects. The Journal of Clinical Pharmacology. 2005;45(12):1400-6.
29. Pastoor D, Gobburu J. Clinical pharmacology review of escitalopram for the treatment of depression. Expert opinion on drug metabolism & toxicology. 2014;10(1):121-8.
30. Renoir T. Selective serotonin reuptake inhibitor antidepressant treatment discontinuation syndrome: a review of the clinical evidence and the possible mechanisms involved. Frontiers in pharmacology. 2013;4:45.
31. Altamura AC, Caldiroli A, Buoli M. Pharmacokinetic evaluation of fluvoxamine for the treatment of anxiety disorders. Expert opinion on drug metabolism & toxicology. 2015;11(4):649-60.
32. Tang SW, Helmeste D. Paroxetine. Expert opinion on pharmacotherapy. 2008;9(5):787-94.
33. Bymaster FP, Dreshfield-Ahmad LJ, Threlkeld PG, Shaw JL, Thompson L, Nelson DL, et al. Comparative affinity of duloxetine and venlafaxine for serotonin and norepinephrine transporters in vitro and in vivo, human serotonin receptor subtypes, and other neuronal receptors. Neuropsychopharmacology. 2001;25(6):871-80.
34. Brent DA, Emslie GJ, Clarke GN, Asarnow J, Spirito A, Ritz L, et al. Predictors of spontaneous and systematically assessed suicidal adverse events in the treatment of SSRI-resistant depression in adolescents (TORDIA) study. American Journal of Psychiatry. 2009;166(4):418-26.
35. Rynn MA, Riddle MA, Yeung PP, Kunz NR. Efficacy and safety of extended-release venlafaxine in the treatment of generalized anxiety disorder in children and adolescents: two placebo-controlled trials. American Journal of Psychiatry. 2007;164(2):290-300.
36. Faquih AE, Memon RI, Hafeez H, Zeshan M, Naveed S. A Review of Novel Antidepressants: A Guide for Clinicians. Cureus. 2019;11(3):e4185.
37. Findling RL, Groark J, Chiles D, Ramaker S, Yang L, Tourian KA. Safety and tolerability of desvenlafaxine in children and adolescents with major depressive disorder. Journal of child and adolescent psychopharmacology. 2014;24(4):201-9.
38. Sansone RA, Sansone LA. Serotonin norepinephrine reuptake inhibitors: a pharmacological comparison. Innovations in clinical neuroscience. 2014;11(3-4):37-42.
39. Spina E, Trifiro G, Caraci F. Clinically significant drug interactions with newer antidepressants. CNS drugs. 2012;26(1):39-67.
40. Dulcan, Mina K. Dulcan's Textbook of Child and Adolescent Psychiatry. Second edition. Arlington, VA: American Psychiatric Association Publishing, 2016.
41. Choy EH, Mease PJ, Kajdasz DK, Wohlreich MM, Crits-Christoph P, Walker DJ, et al. Safety and tolerability of duloxetine in the treatment of patients with fibromyalgia: pooled analysis of data from five clinical trials. Clinical rheumatology. 2009;28(9):1035-44.
42. Keks NA, Hope J, Keogh S, Copolov DL. Milnacipran: serotonin-noradrenaline reuptake inhibitor approved for fibromyalgia may be a useful antidepressant. Australasian Psychiatry. 2018;26(5):537-40.
43. Bakish D, Bose A, Gommoll C, Chen C, Nunez R, Greenberg WM, et al. Levomilnacipran ER 40 mg and 80 mg in patients with major depressive disorder: a phase III, randomized, double-blind, fixed-dose, placebo-controlled study. Journal of psychiatry & neuroscience: JPN. 2014;39(1):40-9.
44. Tallon D, Wiles N, Campbell J, Chew-Graham C, Dickens C, Macleod U, et al. Mirtazapine added to selective serotonin reuptake inhibitors for treatment-resistant depression in primary care (MIR trial): study protocol for a randomised controlled trial. Trials. 2016;17(1):66.
45. Sato H, Ito C, Tashiro M, Hiraoka K, Shibuya K, Funaki Y, et al. Histamine H 1 receptor occupancy by the new-generation antidepressants fluvoxamine and mirtazapine: a positron emission tomography study in healthy volunteers. Psychopharmacology. 2013;230(2):227-34.
46. Mohatt J, Bennett SM, Walkup JT. Treatment of separation, generalized, and social anxiety disorders in youths. American Journal of Psychiatry. 2014;171(7):741-8.
47. Hetrick SE, McKenzie JE, Cox GR, Simmons MB, Merry SN. Newer generation antidepressants for depressive disorders in children and adolescents. Cochrane Database of Systematic Reviews. 2012(11).
48. Stahl SM. Mechanism of action of trazodone: a multifunctional drug. CNS spectrums. 2009;14(10):536-46.
49. Jaffer KY, Chang T, Vanle B, Dang J, Steiner AJ, Loera N, et al. Trazodone for insomnia: A systematic review. Innovations in clinical neuroscience. 2017;14(7-8):24-34.
50. Blackmer AB, Feinstein JA. Management of sleep disorders in children with neurodevelopmental disorders: a review. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2016;36(1):84-98.
51. Owens JA, Rosen CL, Mindell JA, Kirchner HL. Use of pharmacotherapy for insomnia in child psychiatry practice: A national survey. Sleep medicine. 2010;11(7):692-700.
52. Bossini L, Coluccia A, Casolaro I, Benbow J, Amodeo G, De Giorgi R, et al. Off-label trazodone prescription: evidence, benefits and risks. Current pharmaceutical design. 2015;21(23):3343-51.
53. Fagiolini A, Comandini A, Dell'Osso MC, Kasper S. Rediscovering trazodone for the treatment of major depressive disorder. CNS drugs. 2012;26(12):1033-49.
54. Khouzam HR. A review of trazodone use in psychiatric and medical conditions. Postgraduate medicine. 2017;129(1):140-8.

55. Carvalho AF, Sharma MS, Brunoni AR, Vieta E, Fava GA. The safety, tolerability and risks associated with the use of newer generation antidepressant drugs: a critical review of the literature. Psychotherapy and psychosomatics. 2016;85(5):270-88.
56. Stahl SM, Pradko JF, Haight BR, Modell JG, Rockett CB, Learned-Coughlin S. A review of the neuropharmacology of bupropion, a dual norepinephrine and dopamine reuptake inhibitor. Primary care companion to the Journal of clinical psychiatry. 2004;6(4):159-66.
57. Hesse LM, Venkatakrishnan K, von Moltke LL, Duan SX, Shader RI, Greenblatt DJ. CYP2B6 mediates the in vitro hydroxylation of bupropion: potential drug interactions with other antidepressants. Drug Metabolism and Disposition. 2000;28(10):1176-83.
58. Garcia G, Logan GE, Gonzalez-Heydrich J. Management of psychotropic medication side effects in children and adolescents. Child and Adolescent Psychiatric Clinics. 2012;21(4):713-38.
59. Dagan Y, Yager J. Severe bupropion XR abuse in a patient with long-standing bulimia nervosa and complex PTSD. International Journal of Eating Disorders. 2018;51(10):1207-9.
60. Moreira R. The efficacy and tolerability of bupropion in the treatment of major depressive disorder. Clinical Drug Investigation. 2011;31(1):5-17.
61. Daviss WB, Bentivoglio P, Racusin R, BROWN KM, BOSTIC JQ, WILEY L. Bupropion sustained release in adolescents with comorbid attention-deficit/hyperactivity disorder and depression. Journal of the American Academy of Child & Adolescent Psychiatry. 2001;40(3):307-14.
62. Strawn JR, Welge JA, Wehry AM, Keeshin B, Rynn MA. Efficacy and tolerability of antidepressants in pediatric anxiety disorders: a systematic review and meta-analysis. Depression and anxiety. 2015;32(3):149-57.
63. Geller DA, March J, Issues ACoQ. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Obsessive-Compulsive Disorder. Journal of the American Academy of Child & Adolescent Psychiatry. 2012;51(1):98-113.
64. Geller DA, Biederman J, Stewart SE, Mullin B, Martin A, Spencer T, et al. Which SSRI? A meta-analysis of pharmacotherapy trials in pediatric obsessive-compulsive disorder. American Journal of Psychiatry. 2003;160(11):1919-28.
65. Watson HJ, Rees CS. Meta-analysis of randomized, controlled treatment trials for pediatric obsessive-compulsive disorder. Journal of Child Psychology and Psychiatry. 2008;49(5):489-98.
66. GÜNEY SA, ŞAHBUDAK B. Çocuk ve Ergen Psikiyatrisinde Antidepresanlar ve Anksiyolitikler. Turkiye Klinikleri Child Psychiatry-Special Topics. 2017;3(1):8-15.
67. Kasper S, Hamon M. Beyond the monoaminergic hypothesis: agomelatine, a new antidepressant with an innovative mechanism of action. The world journal of biological psychiatry. 2009;10(2):117-26.
68. De Berardis D, Marini S, Fornaro M, Srinivasan V, Iasevoli F, Tomasetti C, et al. The melatonergic system in mood and anxiety disorders and the role of agomelatine: implications for clinical practice. International journal of molecular sciences. 2013;14(6):12458-83.
69. Buoli M, Grassi S, Serati M, Altamura AC. Agomelatine for the treatment of generalized anxiety disorder. Expert opinion on pharmacotherapy. 2017;18(13):1373-9.
70. Plesničar BK. Efficacy and tolerability of agomelatine in the treatment of depression. Patient preference and adherence. 2014;8:603-12.
71. Perlemuter G, Cacoub P, Valla D, Guyader D, Saba B, Batailler C, et al. Characterisation of agomelatine-induced increase in liver enzymes: frequency and risk factors determined from a pooled analysis of 7605 treated patients. CNS drugs. 2016;30(9):877-88.
72. Freiesleben SD, Furczyk K. A systematic review of agomelatine-induced liver injury. Journal of molecular psychiatry. 2015;3(1):4.
73. Baldwin DS, Loft H, Dragheim M. A randomised, double-blind, placebo controlled, duloxetine-referenced, fixed-dose study of three dosages of Lu AA21004 in acute treatment of major depressive disorder (MDD). European Neuropsychopharmacology. 2012;22(7):482-91.
74. Bang-Andersen B, Ruhland T, Jørgensen M, Smith G, Frederiksen K, Jensen KG, et al. Discovery of 1-[2-(2, 4-dimethylphenylsulfanyl) phenyl] piperazine (Lu AA21004): a novel multimodal compound for the treatment of major depressive disorder. Journal of medicinal chemistry. 2011;54(9):3206-21.
75. Alvarez E, Perez V, Dragheim M, Loft H, Artigas F. A double-blind, randomized, placebo-controlled, active reference study of Lu AA21004 in patients with major depressive disorder. International Journal of Neuropsychopharmacology. 2012;15(5):589-600.
76. Jacobsen PL, Mahableshwarkar AR, Serenko M, Chan S, Trivedi MH. A randomized, double-blind, placebo-controlled study of the efficacy and safety of vortioxetine 10 mg and 20 mg in adults with major depressive disorder. The Journal of clinical psychiatry. 2015;76(5):575-82.
77. Mahableshwarkar AR, Jacobsen PL, Serenko M, Chen Y, Trivedi MH. A randomized, double-blind, placebo-controlled study of the efficacy and safety of 2 doses of vortioxetine in adults with major depressive disorder. The Journal of clinical psychiatry. 2015;76(5):583-91.
78. Kaur U, Pathak BK, Singh A, Chakrabarti SS. Esketamine: a glimmer of hope in treatment-resistant depression. European archives of psychiatry and clinical neuroscience. 2019:1-13.
79. Newport DJ, Carpenter LL, McDonald WM, Potash JB, Tohen M, Nemeroff CB, et al. Ketamine and other NMDA antagonists: early clinical trials and possible mechanisms in depression. American Journal of Psychiatry. 2015;172(10):950-66.
80. Han Y, Chen J, Zou D, Zheng P, Li Q, Wang H, et al. Efficacy of ketamine in the rapid treatment of major depressive disorder: a meta-analysis of randomized, double-blind, placebo-controlled studies. Neuropsychiatric disease and treatment. 2016;12:2859-67.
81. Wilkinson ST, Ballard ED, Bloch MH, Mathew SJ, Murrough JW, Feder A, et al. The effect of a single dose of intravenous ketamine on suicidal ideation: a systematic review and individual participant data meta-analysis. American journal of psychiatry. 2017;175(2):150-8.
82. Mathisen LC, Skjelbred P, Skoglund LA, Øye I. Effect of ketamine, an NMDA receptor inhibitor, in acute and chronic orofacial pain. Pain. 1995;61(2):215-20.

83. Oye I, Paulsen O, Maurset A. Effects of ketamine on sensory perception: evidence for a role of N-methyl-D-aspartate receptors. Journal of Pharmacology and Experimental Therapeutics. 1992;260(3):1209-13.
84. Malinovsky J, Servin F, Cozian A, Lepage J, Pinaud M. Ketamine and norketamine plasma concentrations after iv, nasal and rectal administration in children. British Journal of Anaesthesia. 1996;77(2):203-7.
85. Canuso CM, Singh JB, Fedgchin M, Alphs L, Lane R, Lim P, et al. Efficacy and safety of intranasal esketamine for the rapid reduction of symptoms of depression and suicidality in patients at imminent risk for suicide: results of a double-blind, randomized, placebo-controlled study. American journal of psychiatry. 2018;175(7):620-30.
86. Zhu W, Ding Z, Zhang Y, Shi J, Hashimoto K, Lu L. Risks associated with misuse of ketamine as a rapid-acting antidepressant. Neuroscience bulletin. 2016;32(6):557-64.
87. Anderson HD, Pace WD, Libby AM, West DR, Valuck RJ. Rates of 5 common antidepressant side effects among new adult and adolescent cases of depression: a retrospective US claims study. Clinical therapeutics. 2012;34(1):113-23.
88. Hammad TA, Laughren T, Racoosin J. Suicidality in pediatric patients treated with antidepressant drugs. Archives of general psychiatry. 2006;63(3):332-9.
89. Uher R, Farmer A, Henigsberg N, Rietschel M, Mors O, Maier W, et al. Adverse reactions to antidepressants. The British Journal of Psychiatry. 2009;195(3):202-10.
90. Goldstein BJ, Goodnick PJ. Selective serotonin reuptake inhibitors in the treatment of affective disorders—III. Tolerability, safety and pharmacoeconomics. Journal of Psychopharmacology. 1998;12(4_suppl):55-S87.
91. Safer DJ, Zito JM. Treatment-emergent adverse events from selective serotonin reuptake inhibitors by age group: children versus adolescents. Journal of Child & Adolescent Psychopharmacology. 2006;16(1-2):159-69.
92. Wilens TE, Biederman J, Kwon A, Chase R, Greenberg L, Mick E, et al. A systematic chart review of the nature of psychiatric adverse events in children and adolescents treated with selective serotonin reuptake inhibitors. Journal of child and adolescent psychopharmacology. 2003;13(2):143-52.
93. Spigset O. Adverse reactions of selective serotonin reuptake inhibitors. Drug Safety. 1999;20(3):277-87.
94. Murphy TK, Segarra A, Storch EA, Goodman WK. SSRI adverse events: how to monitor and manage. International Review of Psychiatry. 2008;20(2):203-8.
95. Baldessarini RJ, Tondo L, Ghiani C, Lepri B. Illness risk following rapid versus gradual discontinuation of antidepressants. American Journal of Psychiatry. 2010;167(8):934-41.
96. Voican CS, Corruble E, Naveau S, Perlemuter G. Antidepressant-induced liver injury: a review for clinicians. American Journal of Psychiatry. 2014;171(4):404-15.
97. Choi S. Nefazodone (Serzone) withdrawn because of hepatotoxicity. CMAJ. 2003;169(11):1187.
98. Fava M. Weight gain and antidepressants. The Journal of clinical psychiatry. 2000;61:37-41.
99. Zimmermann U, Kraus T, Himmerich H, Schuld A, Pollmächer T. Epidemiology, implications and mechanisms underlying drug-induced weight gain in psychiatric patients. Journal of psychiatric research. 2003;37(3):193-220.
100. Serretti A, Mandelli L. Antidepressants and body weight: a comprehensive review and meta-analysis. The Journal of clinical psychiatry. 2010;71(10):1259-72.
101. Pacher P, Ungvari Z, Nanasi PP, Furst S, Kecskemeti V. Speculations on difference between tricyclic and selective serotonin reuptake inhibitor antidepressants on their cardiac effects. Is there any? Current medicinal chemistry. 1999;6(6):469-80.
102. Sarlon J, Habich O, Schneider B. Elevated rest heart rate in psychiatric patients and different effects of psychotropic medication. Pharmacopsychiatry. 2016;49(01):18-22.
103. Thase ME, Larsen KG, Reines E, Kennedy SH. The cardiovascular safety profile of escitalopram. European Neuropsychopharmacology. 2013;23(11):1391-400.
104. Beach SR, Celano CM, Noseworthy PA, Januzzi JL, Huffman JC. QTc prolongation, torsades de pointes, and psychotropic medications. Psychosomatics. 2013;54(1):1-13.
105. McNally P, McNicholas F, Oslizlok P. The QT interval and psychotropic medications in children. European child & adolescent psychiatry. 2007;16(1):33-47.
106. Whiskey E, Taylor D. A review of the adverse effects and safety of noradrenergic antidepressants. Journal of Psychopharmacology. 2013;27(8):732-9.
107. Goldstein DJ. Duloxetine in the treatment of major depressive disorder. Neuropsychiatric Disease and Treatment. 2007;3(2):193-209.
108. Henry A, Kisicki M, Varley C. Efficacy and safety of antidepressant drug treatment in children and adolescents. Molecular psychiatry. 2012;17(12):1186-93.
109. Dobson ET, Strawn JR. Pharmacotherapy for pediatric generalized anxiety disorder: a systematic evaluation of efficacy, safety and tolerability. Pediatric Drugs. 2016;18(1):45-53.
110. Luft MJ, Lamy M, DelBello MP, McNamara RK, Strawn JR. Antidepressant-induced activation in children and adolescents: risk, recognition and management. Current problems in pediatric and adolescent health care. 2018;48(2):50-62.
111. Goodman WK, Murphy TK, Storch EA. Risk of adverse behavioral effects with pediatric use of antidepressants. Psychopharmacology. 2007;191(1):87-96.
112. Vitiello B, Silva S, Rohde P, Kratochvil C, Kennard B, Reinecke M, et al. Suicidal events in the Treatment for Adolescents with Depression Study (TADS). The Journal of clinical psychiatry. 2009;70(5):741-7.
113. Boyer EW, Shannon M. The serotonin syndrome. New England Journal of Medicine. 2005;352(11):1112-20.
114. Gibbons RD, Brown CH, Hur K, Marcus SM, Bhaumik DK, Erkens JA, et al. Early evidence on the effects of regulators' suicidality warnings on SSRI prescriptions and suicide in children and adolescents. American Journal of Psychiatry. 2007;164(9):1356-63.
115. Wagner KD, Berard R, Stein MB, Wetherhold E, Carpenter DJ, Perera P, et al. A multicenter, randomized, double-blind, placebo-controlled trial ofparoxetine in children and adolescents with social anxiety disorder. Archives of General Psychiatry. 2004;61(11):1153-62.

116. March JS, Entusah AR, Rynn M, Albano AM, Tourian KA. A randomized controlled trial of venlafaxine ER versus placebo in pediatric social anxiety disorder. Biological Psychiatry. 2007;62(10):1149-54.
117. Cipriani A, Zhou X, Del Giovane C, Hetrick SE, Qin B, Whittington C, et al. Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: a network meta-analysis. The Lancet. 2016;388(10047):881-90.